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## Low Molecular Wt Heparins:

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**- Discussion:**

- anti-Xa to anti IIa ratio for enoxaparin is about 3 to 1 whereas unfractionated heparin has a ratio of 1 to 1;
  - hence LMWH has a greater inhibitory effect on factor Xa and has a lesser effect on thrombin;
- thrombocytopenia and platelet dysfunction seems to occur less often than w/ unfractionated heparin;

**- Adult Dose:**

- 30 mg SQ bid;

**- Labs:**

- because LMWH have minimal effect on thrombin, there is minimal elevation of the PTT;

**- Lovenox / Enoxaparin:**

- subcutaneous enoxaparin 30 mg every 12 hours;
- onset of activity occurs after about 3 hours;
- it is advised to delay administration of Lovenox for 12-24 hours following surgery;
- renal excretion is the main route of removal, and therefore dose reduction is required w/ significant renal dysfunction;
- in a total hip arthroplasty study by Colwell et al (JBJS July 1999, Vol 81-A), the overall rate of thromboembolic disease was 3.7 % for patients receiving adjusted dose coumadin;
  - rate of clinically significant bleeding was 0.9%;
  - lovenox was continued only for the length of the hospitalization which averaged about 7 days;
- in the study by Hans Klaus Breddin et al. 2001, the authors performed a multicenter, open-label study with blinded adjudication of end points w/ randomly assigned patients with acute DVT to one of three treatment regimens: intravenous administration of unfractionated heparin;
  - subcutaneous administration of a low-molecular-weight heparin, reviparin, twice a day for one week; or subcutaneous administration of reviparin once a day for four weeks.
  - primary end point was evidence of regression of the thrombus on venography on day 21; secondary end points were recurrent venous thromboembolism, major bleeding within 90 days after enrollment, and death;
  - of the patients receiving unfractionated heparin, 40.2 percent (129 of 321) had thrombus regression, as compared with 53.4 percent (175 of 328) of the patients receiving reviparin twice daily and 53.5 % (167 of 312) of the patients receiving reviparin once daily;
  - w/ regard to thrombus regression, reviparin administered twice daily was significantly more effective than heparin (relative likelihood of thrombus regression, 1.28; 97.5 percent confidence interval, 1.08 to 1.5); reviparin administered once daily (relative likelihood, 1.29; 97.5 percent confidence interval, 1.08 to 1.5).
  - in acute deep-vein thrombosis, reviparin regimens are more effective than unfractionated heparin in reducing the risk of recurrent thromboembolism;
  - ref: Effects of a Low-Molecular-Weight Heparin on Thrombus Regression and Recurrent Thromboembolism. Hans Klaus Breddin et al. N Engl J Med 2001;344:626-31.

**- Pentasaccharides:**

- in the report by G.G Alexander et al., the authors studied the effects of the pentasaccharide Org31540/SR901, a highly selective, indirect inhibitor of activated factor X, is the first of a new class of synthetic antithrombotic agents.
- in a double-blind study, patients were randomly assigned to postoperative administration of one of five different doses of Org31540/SR90107A, given once daily, or to 30 mg of enoxaparin, given every 12 hours;
- treatment was continued for 10 days or until bilateral venography was performed after a minimum of 5 days;
- of 933 patients treated, 593 were eligible for the efficacy analysis;
- with Org31540/SR90107A a dose effect was observed ( $P=0.002$ ), with rates of venous thromboembolism of 6.7 %, 1.7 %, 4.4 %, and 0 % for the groups assigned to 0.75 mg, 1.5 mg, 3.0 mg, 6.0 mg, and 8.0 mg of the drug, respectively, as compared with a rate of 9.4 % in the enoxaparin group;
- reduction in the risk of venous thromboembolism was 82 percent for the 3.0-mg Org31540/SR90107A group and 29 percent for the 1.5-mg group ( $P=0.51$ );
- enrollment in the 6.0-mg and 8.0-mg Org31540/SR90107A groups was discontinued because of bleeding;
- major bleeding occurred 3.5 percent less frequently in the 0.75-mg group ( $P=0.01$ ) and 3.0 percent less frequently in the 1.5-mg group ( $P=0.05$ ) than in the enoxaparin group (in which the rate was similar to that in the control group);
- the authors concluded that Org31540/SR90107A, a synthetic pentasaccharide, has the potential to improve the safety and efficacy ratio for the prevention of venous thromboembolism, as compared with low-molecular-weight heparin.

- ref: A Synthetic Pentasaccharide for the Prevention of Deep-Vein Thrombosis after Total Hip Replacement  
G.G Alexander et al. The New England Journal of Medicine -- March 1, 2001 -- Vol. 344, No. 9

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Low-molecular-weight heparinoid compared with warfarin for prophylaxis of DVT in patients who are operated on  
Prevention of DVT and PE after THR. Comparison of low-molecular-weight heparin and unfractionated heparin.  
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CW Colwell et al JBJS July 1999, Vol 81-A, No 7.